intracerebrally transferred ginsenoside Rb_1.

As described in JP98/365560 and PCT/JP99/02550 ("Brain cell or nerve cell-protective agents comprising ginsenoside Rb_1"), intravenous administration of ginsenoside Rb_1 can reduce the infarcted area to about 1/4 in comparison with that of a non-administered control group, as well as having a unique action mechanism that is to enhance the expression of a cell death-suppressing factor Bcl-X_L. It also protects nerve cells or neurons in the brain. Consequently, it can be applied as neuroprotective agents for not only acute and chronic cerebral infarction (cerebral thrombosis or cerebral embolism) but also acute phase or chronic phase of cerebral hemorrhage and subarachnoidal hemorrhage or transient cerebral ischemic attack. Namely, ginsenoside Rb_1, which does not promote bleeding tendency, is the drug or pharmaceutical composition, which can be administered intravenously by drip infusion in an ambulance car to a patient suspected to suffer from cerebral apoplexy. Administration of ginsenoside Rb_1 to patients with cerebral infarction before thrombolytic therapy would ameliorate prognosis of the patients.

In addition, ginsenoside Rb_1 of the present invention can not only reduce the infarcted area to about 1/4 as a result of intravenous administration for a maximum of 28 days, but can also cause recovery of the damaged and reduced vascular networks

in the ischemic penumbra to almost a normal state. Consequently, intravenous administration of ginsenoside Rb_1 stimulates the regeneration and/or reconstruction of the damaged and/or reduced cerebrovascular networks after cerebral apoplexy, and once rescued by intavenous administration of ginsenoside Rb_1 the brain tissues in the ischemic penumbra can function in a normal manner presumably for good even after the termination of intravenous administration of the pharmaceutical composition or drug. Ginsenoside Rb_1 of the present invention is expected to protect the injured or damaged brain through an indirect and long term protective mechanism that is to facilitate the regeneration and reconstruction of cerebrovascular networks, and also provides a direct protective effect on nerve cells through enhancement of the expression of Bcl-X_L protein and suppression of apoptosis-like nerve cell death. As such, ginsenoside Rb_1 appears to be the first compound, in the world which can reduce the infarcted area to about 1/4 by intravenous infusion, not only during the acute phase of cerebral infarction, but also at one month after the onset of cerebral infarction. Consequently, in the future, various protective agents for brain cells or nerve cells may be newly developed by using ginsenoside Rb_1 or its metabolites as a leading compound(s).

In the general clinical field, there are many cases, in which the higher nervous function is continuously deteriorated even though no new ischemic brain attack is noted after the first

onset of cerebral infarction. Especially there are cases with continuously deteriorating sequelae after cerebral apoplexy. A reason for this may be that the regeneration or reconstruction of the damaged or reduced cerebrovascular networks caused by cerebral apoplectic attack (brain attack) is sometimes insufficient. Intravenous administration or nasal administration of ginsenoside Rb_1 is expected to exhibit conspicuous effects in ameliorating such sequelae after cerebral apoplexy.

Since the intravenous administration of ginsenoside Rb_1 of the present invention exhibits a novel effect and efficacy in promoting vascular regeneration and/or reconstruction, it may also be effective for treatment of other diseases with symptoms of blood flow disorders (e.g. aortitis syndrome, acute peripheral arterial embolism, thromboangitis obliterans, arteriosclerosis obliterans, Raynaud's disease or Raynaud's syndrome). The efficacy of ginsenoside Rb_1 to inhibit cell death in tissues suffering from blood flow disorders and in diseases with major symptoms of these blood flow disorders should be kept in mind. Consequently, ginsenoside Rb_1 is expected to reduce tissue injuries resulting from blood flow disorders of the peripheral tissues through at least two action mechanisms.

Since the pharmaceutical composition comprising ginsenoside Rb_1 inhibits the development of secondary lesions